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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,850	AVIDES ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,20,22,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *5,9-11,13-17,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-8,12,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence comparisons*.

Avides et al.

DETAILED ACTION

Election/Restrictions

The Election filed on 2/28/2006 in response to the Restriction Requirement of 12/08/2006 has been entered. Applicant's election of Group I, claims 1-4, 6-8 and 12, as specifically drawn to the special technical feature of a polynucleotide has been acknowledged.

Applicant's election with traverse of Group I is acknowledged. The traversal is on the ground(s) that the requirement itself is in conflict with the finding of unity of invention during the international stage, wherein no objection as to lack of unity was raised during the international phase of in the international application in which this case is a 35 USC 371 national phase application. As such, Applicants submit that PCT Article 27 provides that it is improper for national offices to require compliance with the requirements relating to the form or contents of the application different from or additional to those which are provided for in the PCT. Moreover, Applicants contend that the MPEP 1850 states that ... when the Office considers international applicants as an International Searching Authority, as an International Examining Authority, and during the national state as a Designated or Elected Office under 35 USC 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 USC 111. (emphasis added). Indeed, Applicants assert that the same standard for unity of invention is applicable to both international applications and national phase applications. Furthermore, Applicants submit that, minimally, Groups I and II form a single general inventive concept and thereby possess unity of invention. For example, Applicants direct the Examiners attention to the WIPO "PCT International Search and Preliminary Examination Guidelines" (2004), Example 39 (see Chapter 10.59) which provides an example of claims drawn to an isolated protein X and an isolated nucleic acid encoding protein X, wherein the claims were found to have unity of invention because protein X makes a contribution over the prior art, protein X and the DNA encoding protein X share a special technical feature. Accordingly, Applicants submit that in accordance with PCT Rule 13.1, as evidenced by the WIPO Guidelines, at least Groups I and II possess unity of invention and minimally, should be rejoined for the purpose of the initial examination because both Groups I and II are directed to nucleotide and polypeptide sequences. In addition, Applicants submit that the US Patent Office has already indicated that the

search of multiple sequences are acceptable see MPEP 1850 "Unity of Invention-Nucleotide Sequences" which stats that "the Commissioner has decided sua sponte to partially wave 37 1.475 and 1.499 et seq. to permit applicants to claim up to ten (10) nucleotide sequences that do not have the same or corresponding technical feature." Accordingly, Applicants submit that while Groups I and II are directed to a nucleotide and amino acid sequence, respectively, examination of two sequences in the same application would be appropriate and within the spirit of MPEP 1850.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants contention that the it is improper to find a lack of unity in a 35 USC 371 application when no objection was raised during the international phase of the international application, the Examiner acknowledges that no objection to lack of unity was raised during the international phase of the application. However, the Examiner recognizes that while the international phase of examination are useful for determining the patentability of the international application, the instantly filed application is treated as a new and/or distinct application. In response to Applicants submission that in view of PCT Rule 13.1 and Example 39 of the WIPO "PCT International Search and Preliminary Examination Guidelines" (2004) Groups I and II possesses unity of invention, the Examiner acknowledges and agrees with Applicants assertion that when a protein X makes a contribution over the prior art, protein X and the DNA encoding protein X share a special technical feature. However, the Examiner recognizes that the special technical feature appears to be an isolated polynucleotide molecule encoding orbit or a homologue thereof. In the instant case, the specification teaches that homologous sequences are taken to include an amino acid sequence that is at least 15, 20, 25, 30, 40, 50, 60, 70, 80 or 90% identical, preferably 95 or 98% identical at the amino acid level over at least 50 or 100, preferably 200, 300, 400 or 500 amino acids with SEQ ID NO: 2 (page 7, lines 22-25). In view of this, the isolated polynucleotide disclosed in the NCBI database for single nucleotide polymorphism (National Center for Biotechnology Information, National Library of Medicine, NIH (Bethesda, MD, USA) having the accession # AB014522 submitted on 2/06/1999 which encodes a polypeptide that has 18.1% total similarity and 30.1% local similarity from amino acids 236 to 1492 of the amino acid sequence of SEQ ID NO: 2 meets the limitation of a homologue of orbit as defined by the specification (see specification page 14, lines 18-25 for disclosure of accession numbers). Therefore, the technical

feature linking the inventions of Groups I-X does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-17, 20, 22 and 25-26 are currently pending

Claims 5, 9-11, 13-17, 20 and 22 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1-4, 6-8, 12 and 25-26 are currently under consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on 07/13/1999 and 12/24/1999. It is noted, however, that applicant has not filed a certified copy of the 9916402.2 and 9931707.6 applications as required by 35 U.S.C. 119(b). As such, the Examiner has established a priority date of **07/11/2000** consistent with the filing date of the PCT application. If applicant disagrees with any rejection of claims 1-4, 6-8, 12 and 25-26 set forth in this office action based on examiner's establishment of a priority date of **7/11/2000** for the instant claims in application serial number 10/030,850 applicant is invited to submit certified copies of the 9916402.2 and 9931707.6 applications establishing an earlier priority date.

Information Disclosure Statement

The Information Disclosure Statement filed on 02/28/2005 has been acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The disclosure is objected to because of the following informalities:

The specification on page 1 should be amended to reflect the priority status of the present application, for example: The present application is a 371 of PCT/GB00/02662 filed on 07/11/200 which claims the benefit of priority of United Kingdom application Nos: 9916402.2 and 9930707.6 filed on 07/13/1999 and 12/24/1999 respectively, the entire contents of which are incorporated herein by reference.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 12, as written, does not sufficiently distinguish over polynucleotides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught in preceding claims 1-3. See MPEP 2105.

Claims 1-4, 11,14-15, and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a substantial utility.

(Note: Because Applicants have not disclosed a substantial utility for the claimed invention, credibility will not be assessed.

The current claims are drawn to a polynucleotide sequence which encodes a orbit protein or homolog thereof, wherein the polynucleotide sequence comprises the nucleotide sequence of SEQ ID NO: 1 and the orbit protein comprises the amino acid sequence of SEQ ID NO: 2.

The specification teaches the identification and isolation of genomic and cDNA clones comprising the nucleotide sequence of SEQ ID NO: 1 which encode a novel protein from *Drosophila* referred to as "orbit" having an amino acid sequence of SEQ ID NO: 2, wherein the orbit protein has been found to localize to mitotic spindles and bind microtubules (page 3, lines 13-16). The specification asserts that the orbit polypeptide or homologue, derivative, variant, or fragment thereof can be used in an assay for identifying a substance that is capable of affecting orbit function, i.e. inhibiting mitosis (page 5, lines 23-27). The specification further asserts that the polynucleotides, polypeptides, or antibodies can be in the form of a kit which can be used for diagnosing the presence of or absence of obit or their homologs (page 5, lines 9-11). The specification also asserts that the polynucleotides, polypeptides or antibodies of the invention can be used in method of treating a tumor (page 6, lines 24-26).

A search of the prior art indicates that an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1, which encodes an "orbit" polypeptide having the amino acid sequence of SEQ ID NO: 2 is novel and non-obvious. The closest "human" polynucleotide and/or polypeptide is disclosed by Ishikawa et al. (DNA Res. 1998; 5: 169-176, Accession # KIAA062 for the polypeptide) which is referenced in the specification (page 39, lines 26-30 and Figure 2) as having a region 35% identical (48% similar) from residue 290 to residue 1068 of orbit, e.g. SEQ ID NO: 2, wherein the cDNA clones are referenced in the specification as having an unknown function (page 11, lines 10-12).

Substantial Utility

Following the requirements of the Utility Guidelines (http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf), "substantial utility" is a utility that defines a "real world use", wherein utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. Here, the evidence in the specification provided is that the instantly claimed nucleic acid encodes a protein in *Drosphila* referred to as orbit which has been found to localize to mitotic spindles and bind microtubules. However, the specification fails to show any correlation between a polynucleotide isolated in a fruit fly, e.g., Drosphilia, which encodes a protein capable of localizing to mitotic spindles and binding to microtubules and polynucleotides involved in cancer. For example, the specification teaches that the

nucleotide sequences of human KIAA0622 and/or KIAA0627 proteins described by Ishikawa et al., which are described in the specification on page 11, lines 10-12 as having an unknown function, may be used to identify other primate/mammalian homologues since nucleotide homology between human sequences and mammalian sequences is likely to be higher than in the case for the Drosophila sequence identified herein (page 14, lines 1-6).

Regarding the identification of homologues, there is an abundance of evidence that very similar proteins can perform very different functions and that "some" homology is not direct evidence sufficient to impute any utility to the protein and/or polynucletide. For example, Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Further, Scott et al (Nature Genetics, 1999, 21:440-443) teach that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport proteins that included a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter, and 45% similarity to the human sulfate transporter 'downregulated in adenoma'. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al. suggest that these results underscore

the importance of confirming the function of newly identified gene products even when the database searches reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph). These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein.

In addition, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2).

Moreover, the specification does not appear to provide a relationship between the expression pattern of SEQ ID No: 1 or 2 to any specific diseases for the purposes of diagnosis, or show how the expression of SEQ ID NO: 2 via gene therapy would be utilized as a means to treat cancer as intended. The specification does not provide any guidance in terms of what expression patterns are needed for diagnosing and what ends points are required for the treatment of cancer.

Since the specification has failed to establish a real world use of the claimed polynucleotide or treatment containing the polynucleotide, a substantial utility has not been clearly set forth. Hence, further research would be required to identify and reasonable confirm the "real world" use for SEQ ID NO: 1. As noted in the utility guidelines, basic research on a product to identify properties and intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility Guidelines Training Materials).

Claims 1-4, 11,14-15, and 18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections – 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4, 7, 8, 12 and 26 are rejected as vague and indefinite for reciting the term orbit as the sole means of identifying the claimed molecule. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify orbit, for example, by SEQ ID NO: and function of orbit.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4, 6-8, 12 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claims 1 and 6 have been amended to recite an isolated polynucleotide encoding orbit or a homologue thereof, or a complement thereof. While the specification teaches that orbit polypeptides includes homologous sequences obtained from any source, for example, related viral/bacterial, cellular homologues and synthetic peptides, as well as variants or derivatives thereof (page 7, lines 6-10), the specification as originally filed does not appear to have support for the limitation "complement thereof" in the context of an orbit polypeptide. Applicant is invited to point to clear support or specific examples of the claimed limitation in the specification as-filed or remove such amendatory language in response to this office action.

Claims 1-4, 6-8, 12 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of polynucleotide that encodes a polypeptide referred to as orbit or a homolog thereof. Moreover, the claims are inclusive a genus of polynucleotides comprising the nucleotide sequence set forth in SEQ ID NO: 1 including, but not limited to, nucleotide sequence which are capable of hybridizing to SEQ ID NO: 1, nucleotides which are degenerate as a result of the genetic code, polynucleotides having 75% identity to the entire nucleotide sequence set forth in SEQ ID NO: 1 and complements thereof. However, the written description in this case only sets forth one species of polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and a polynucleotide which is a complete complement of the nucleotide sequence set forth in SEQ ID NO: 1.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical

properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

A search of the prior art indicates that an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1, which encodes an "orbit" polypeptide having the amino acid sequence of SEQ ID NO: 2 is novel and non-obvious.

The specification teaches (page 3, lines 13-15) that the specific polynucleotides of the invention include, but are not limited to, isolated genomic and cDNA encoding a protein in *Drosophila* termed orbit. Specifically, the specification teaches that that polypeptides of the invention are not limited to polypeptides having the amino acid sequence set out in SEQ ID NO: 2 or fragments thereof, but also include homologous sequences obtained from any source, for example, related viral/bacterial, cellular homologues and synthetic peptides, as well as variants or derivatives thereof (page 7, lines 6-10). With regards to the homologous sequences, the specification teaches that homologous sequences are taken to include an amino acid sequence that is at least 15, 20, 25, 30, 40, 50, 60, 70, 80 or 90% identical, preferably 95 or 98% identical at the amino acid level over at least 50 or 100, preferably 200, 300, 400 or 500 amino acids with SEQ ID NO: 2 (page 7, lines 22-25). The specification further teaches (page 13, lines 23-24page 14, lines 11-12 and 27-30) that the polynucleotides of the invention include not only polynucleotides comprising the nucleotide sequence of SEQ ID NO: 1, but also, any variant, homologue or derivative thereof, wherein the homology is preferably at least 50% or 75%, more preferably at least 85%, more preferably at least 90% or 95% or 98% homology to the sequence listing herein. Thus, while the specification contemplates homologues polypeptides, specifically human homologues of a orbit polypeptide, i.e. SEQ ID NO: 2 and further, homologues, variants and derivatives thereof of the polynucleotide of SEQ ID NO: 1, the written description only reasonably conveys one species of polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and a polynucleotide which is a complete complement of the nucleotide sequence set forth in SEQ ID NO: 1. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the

genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of polynucleotides which encode a genus of orbit polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only one species of polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and

a polynucleotide which is a complete complement of the nucleotide sequence set forth in SEQ ID NO: 1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the nature of the invention, (2) the relative skill of those in the art, (3) the breadth of the claims, (4) the amount or direction or guidance presented, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the state of the prior art, and (8) the predictability or unpredictability of the art.

Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the

determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406) Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

The nature of the invention

The claim are drawn to a polynucleotide which encodes an orbit polypeptide or homologue thereof or to a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 for use in therapy. The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Level of skill in the art

The level of skill in the art is deemed to be high, generally that of a PhD or MD.

The breadth of the claims

Applicants broadly claim a polynucleotide which encodes an orbit polypeptide or homologue thereof or to a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 for use in therapy. As such, the claims encompass the use of a polynucleotide for the treatment of a condition, which implies gene therapy.

Guidance in the specification and Working Examples

The specification teaches that genomic and cDNA clones which encode a novel protein in Drosophila, termed orbit, have been isolated, wherein the orbit protein has been found to localize to mitotic spindles and bind to microtubules (page 3, lines 13-16). As such, the specification teaches

that since orbit appears to be required for the normal mitotic process, it appears a target for inhibition of cell division, particularly in tumors cells (page 33, lines 3-6). For example, the specification teaches that one possible therapeutic approach is to express anti-sense orbit constructs, preferably selectively in tumor cells, to inhibit orbit function and prevent tumour cell division by means of gene therapy (page 33, lines 8-9). The specification further teaches that the polynucleotides/vectors encoding polypeptide components (or antisense constructs) for inhibiting mitosis may be administered directly as a naked nucleic acid, wherein the polynucleotide or vector is combined with a pharmaceutically acceptable carrier (page 33, lines 30+). Aside from the prophetic embodiments of the disclosure, the specification provides little guidance to one of skill in the art in terms of how to make or use the instantly claimed invention. The specification does not contain any teachings that address the ability of the composition to treat a human subject or even its ability to work *in vivo*. Specifically, the specification has not taught an appropriate tested dose for humans, the amount necessary for successful treatment, the number of cells to be treated, the number of times the treatment needs to be administered or the most appropriate route of administration. Therefore, coupled with the unpredictability of using polynucleotides for the treatment or prevention of a disorder, as underscored by the prior art, the criticality of providing workable examples in an unpredictable art, such as gene therapy, is required for the practice of the instant invention.

Quantity of experimentation

The quantity of experimentation in the areas of gene therapy is extremely large given the unpredictability associated with treating a condition by administering a polynucleotide.

The unpredictability of the art and the state of the prior art

The state of the art at the time of filing was such that one of skill could recognize the unpredictability of treating a disease by a method of gene therapy. For example, gene therapy comprising the administration of recombinant nucleic acids involving *in vivo* or *ex vivo* methods had not seen any success despite a great deal of work and resources. Several reviews in the art show that difficulties with vector selection, mode of delivery and persistence of predictable and effective levels of expression of the protein, created technical barriers to the practice of gene therapy methods. Verma et al states that, "[t]he Achilles heel of gene therapy is gene delivery...", and that, "most of

the approaches suffer from poor efficiency of delivery and transient expression of the gene" (Verma et al. (1997) Nature Volume 389, page 239, column 3, paragraph 2). Marshall concurs, stating that, "difficulties in getting genes transferred efficiently to target cells- and getting them expressed-remain a nagging problem for the entire field", and that "many problems must be solved before gene therapy will be useful for more than the rare application" (Marshall (1995) Science, Volume 269, page 1054, column 3, paragraph 2, and page 1055, column 1).

Numerous factors complicate the gene therapy art which have not been shown to be overcome by routine experimentation. Eck et al. (Goodman & Gilman's The Pharmacological Basis of Therapeutics (1996), 9th Edition, Chapter 5, McGraw-Hill, NY) explains, "the delivery of exogenous DNA and its processing by target cells requires the introduction of new pharmakinetic paradigms beyond those that describe the conventional medicines in use today". Eck et al teaches that with *in vivo* gene transfer, one must account for the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell or its secretory fat, once produced. These factors differ dramatically based on the vector used, the protein being produced and the disease being treated (see Eck et al, bridging pages 81-82).

Also among the many factors that the art teaches affect efficient gene delivery and sustained gene expression are, immune responses and the identity of the promoter used to drive gene expression. Verma et al teaches, in reference to *ex vivo* methods, that weak promoters produce only low levels of therapeutically effective protein, and that only by using appropriate enhancer-promoter combinations can sustained levels of therapeutically effective protein be achieved (Verma et al, *supra*, page 240, column 2). Verma et al further warns that, "...the search for such combinations is a case of trial error for a given cell type" (Verma et al, *supra*, page 240, bridging sentence of columns 2-3). The state of the art is such that no correlation exists between successful expression of a gene and a therapeutic result (Ross et al, Human Gene Therapy,1996, Volume 7, pages 1781-1790, see page 1789, column 1, first paragraph). Thus, the art at the time at the time of filing clearly establishes that

expectation for achieving a desired therapeutic effect in vivo by expressing a therapeutic gene using any of the expression constructs known in the art was extremely low.

More recently, Rubanyi (Mol. Aspects Med. (2001) 22:113-142) teaches that the problems described above remain unresolved. Rubanyi states, "[a]lthough theoretical advantages of [human gene therapy] are undisputable, so far [human gene therapy] has not delivered the promised results: convincing clinical efficacy could not be demonstrated yet in most of the trials conducted so far..." (page 113, paragraph 1). Among the technical hurdles that Rubanyi teaches remain to be overcome are problems with gene delivery vectors and improvement in gene expression control systems (see "3. Technical hurdles to be overcome in the future", beginning on page 116 and continued through page 125). Furthermore, Juengst (British Medical Journal (2003) Volume 326, pages 1410-1411) teaches the unpredictable nature of gene therapy and that a few of the apparent successes actually developed T cell-acute lymphoblastic leukemia due to insertional mutagenesis at or near the LMO-2 gene causing altered gene expression. The art has demonstrated that a large amount of experimentation has already been performed without demonstrating successful gene therapy methods for treatment of disease.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the lack of guidance provided in the specification for in vivo success, and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as written.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 6-8 and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Inoue et al. (J. Cell Biol. 2000; 149: 153-165, IDS).

Inoue et al. teach an isolated polynucleotide molecule referred to as orbit which encodes a conserved 165-kD microtubule-associated protein (MAP) with GTP binding motifs (Abstract). The reference further teaches polynucleotide probes comprising a fragment of at least 1.5 kB of orbit (page 154, 2nd column, P Element Mediated Resue). Moreover, the reference teaches both a vector comprising said polynucleotide as well as an expression vector comprising said orbit polynucleotide (page 154, 2nd column, P Element Mediated Rescue and page 155, 1st paragraph, Orbit Antibody and Western Blot Analysis). Thus, while Inoue et al. do not explicitly recite that the polynucleotide can be used in therapy, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Claims 1, 3, 6, 12 and 25 are rejected under 35 U.S.C. 102(a) as being anticipated by GenEmbl database for nucleotide sequences (Accession Number AB031048, 4/7/2000).

GenEmbl provides an isolated polynucleotide referred to as orbit which appears to be 100% identical to the instantly claimed polynucleotide of SEQ ID NO: 1 (see sequence comparison below). Moreover, the database provides the amino acid sequence for which the polynucleotide encodes that appears to be 100% identical to the obit protein, i.e., SEQ ID NO: 2 encoded by the instantly claimed polynucleotide. Thus, while the GenEmbl database does not explicitly recite that the polynucleotide can be used in therapy, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

```
DEFINITION  Drosophila melanogaster orbit mRNA for microtubule
            associated-protein orbit, complete cds.
ACCESSION   AB031048
VERSION     AB031048.1  GI:7527325
KEYWORDS    microtubule associated-protein orbit.
SOURCE      Drosophila melanogaster (fruit fly)
  ORGANISM  Drosophila melanogaster
            Eukaryota; Metazoa; Arthropoda; Hexapoda; Insecta; Pterygota;
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REFERENCE   1  (sites)
  AUTHORS   Inoue,Y.H., do Carmo Avides,M., Shiraki,M., Deak,P., Yamaguchi,M.,
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  TITLE     Orbit, a novel microtubule-associated protein essential for
mitosis
            in Drosophila melanogaster
  JOURNAL   J. Cell Biol. 149 (1), 153-166 (2000)
   PUBMED   10747094
REFERENCE   2  (bases 1 to 5959)
  AUTHORS   Inoue,Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (11-AUG-1999) Yoshihiro H Inoue, Kyoto Institute of
            Technology, Drosophila Genetic Resource Centre; Matsugasaki,
Sakyo,
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ORIGIN

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Qy 2429 TGATGAGTCTGATGACATCGACTCCGAGGCCAGTTCTGTGTGTTCAGAACGATCTTTCGA 2488
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Db 3133 TGATGAGTCTGATGACATCGACTCCGAGGCCAGTTCTGTGTGTTCAGAACGATCTTTCGA 3192

Qy 2489 CTCCAGCTACACTAGAGGTAATAAATCGAACTACTCACTTAGCGGGAGCCACACCCGCTT 2548
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Db 3193 CTCCAGCTACACTAGAGGTAATAAATCGAACTACTCACTTAGCGGGAGCCACACCCGCTT 3252

Qy 2549 GGACTGGAGCACGCAGCGGGCGCCATTTGACGACATCGAGACGATTATTCAGTTCTGCGC 2608
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 3253 GGACTGGAGCACGCAGCGGGCGCCATTTGACGACATCGAGACGATTATTCAGTTCTGCGC 3312

Qy 2609 ATCGACGCATTGGTCTGAAAGGAAGGATGGCCTGATCAGCCTCACACAGTATCTGGCCGA 2668
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 3313 ATCGACGCATTGGTCTGAAAGGAAGGATGGCCTGATCAGCCTCACACAGTATCTGGCCGA 3372

Qy 2669 TGGAAAGGAGCTCACTCAGCAGCAACTTAAATGCGTTCTGGACATGTTCCGCAAGATGTT 2728
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Db 3373 TGGAAAGGAGCTCACTCAGCAGCAACTTAAATGCGTTCTGGACATGTTCCGCAAGATGTT 3432

Qy 2729 CATGGATACACACACCAAGGTGTACTCACTGTTTTTGGACACGGTCACCGAACTGATTCT 2788
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 3433 CATGGATACACACACCAAGGTGTACTCACTGTTTTTGGACACGGTCACCGAACTGATTCT 3492

Qy 2789 GGTTCATGCGAACGAAACTTCACGAAATGGCTCTTCATCTTGTTTGACGCGGTTGTTCAA 2848
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Db 3493 GGTTCATGCGAACGAAACTTCACGAAATGGCTCTTCATCTTGTTTGACGCGGTTGTTCAA 3552

Qy 2849 CAAATTGGGCACCGATCTACTCAATTCGATGCACAGCAAGATTTGGAAGACGCTACAGGT 2908
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 3553 CAAATTGGGCACCGATCTACTCAATTCGATGCACAGCAAGATTTGGAAGACGCTACAGGT 3612

Qy 2909 GGTCCACGAATATTTCCCCACGCAGTTGCAGCTTAAAGAACTATTTAGAATCATATCGGA 2968
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 3613 GGTCCACGAATATTTCCCCACGCAGTTGCAGCTTAAAGAACTATTTAGAATCATATCGGA 3672

Qy 2969 TTCTACTCAAACGCCAACTACCAAGACGCGCATCGCCATTCTGCGCTTCCTTACGGATCT 3028
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Db 3673 TTCTACTCAAACGCCAACTACCAAGACGCGCATCGCCATTCTGCGCTTCCTTACGGATCT 3732

Qy 3029 GGCCAATACATACTGTAAAAGCAGCGACTTTCCCAGCGACCAGAGCCAGGCCTGCGAGCG 3088
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Db 3733 GGCCAATACATACTGTAAAAGCAGCGACTTTCCCAGCGACCAGAGCCAGGCCTGCGAGCG 3792

Qy 3089 GACGGTCCTAAAGCTGGCCCAGCTGGCGGCGGATCAGAAGTCGATGGAGCTGCGCTCCCA 3148
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Db 3793 GACGGTCCTAAAGCTGGCCCAGCTGGCGGCGGATCAGAAGTCGATGGAGCTGCGCTCCCA 3852

Qy 3149 GGCCAGGAGCTGCCTAGTGGCCCTGTATAACCTGAATACCCCGCAAATGACCCTTTTACT 3208
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Db 3853 GGCCAGGAGCTGCCTAGTGGCCCTGTATAACCTGAATACCCCGCAAATGACCCTTTTACT 3912

Qy 3209 GGCCGACCTGCCAAAGGTATATCAGGACTCTGCCCGATCCTGCATCCATTCGCACATGAG 3268
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Db 3913 GGCCGACCTGCCAAAGGTATATCAGGACTCTGCCCGATCCTGCATCCATTCGCACATGAG 3972

Qy 3269 GCGGCAAAGCCAAAGTTGCAATTCGGGTGCCAATTCGCCTAGTAGCTCTCCATTGAGCAG 3328
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 3973 GCGGCAAAGCCAAAGTTGCAATTCGGGTGCCAATTCGCCTAGTAGCTCTCCATTGAGCAG 4032
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Qy 3329 TAGCAGTCCCAAGCCTTTGCAAAGTCCCTCTGTGGGTCCATTTGCCTCGCTTCAGAGCCA 3388
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Db 4033 TAGCAGTCCCAAGCCTTTGCAAAGTCCCTCTGTGGGTCCATTTGCCTCGCTTCAGAGCCA 4092

Qy 3389 CCACCACCAACTTAGCATCAGCTCTACTAGTCCACGCTCCCGGCAGTCTTCCGTGGAGCA 3448
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Db 4093 CCACCACCAACTTAGCATCAGCTCTACTAGTCCACGCTCCCGGCAGTCTTCCGTGGAGCA 4152

Qy 3449 GGAGCTGCTCTTTTCCTCGGAGCTGGACATTCAGCACAACATTCAGAAGACGTCGGAGGA 3508
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Db 4153 GGAGCTGCTCTTTTCCTCGGAGCTGGACATTCAGCACAACATTCAGAAGACGTCGGAGGA 4212

Qy 3509 GATCCGGCACTGCTTCGGCGGTCAGTACCAGACGGCGCTGGCGCCCAATGGCTTCAATGG 3568
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Db 4213 GATCCGGCACTGCTTCGGCGGTCAGTACCAGACGGCGCTGGCGCCCAATGGCTTCAATGG 4272

Qy 3569 ACACTTGCAGTATCACGATCAGGGCCAACAGGATTCGTGTGCATCCCTGTCTTCCAACTC 3628
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Db 4273 ACACTTGCAGTATCACGATCAGGGCCAACAGGATTCGTGTGCATCCCTGTCTTCCAACTC 4332

Qy 3629 CAAGACGCAATCGTCGGCCAACACTACCCAGTCAAATACACCTGAGTCAGCAACAATGAG 3688
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Db 4333 CAAGACGCAATCGTCGGCCAACACTACCCAGTCAAATACACCTGAGTCAGCAACAATGAG 4392

Qy 3689 GCTGGATAATCTGGAGCGGGAAAGGACCACTCAGAACGCCAAGTCACCAACTGACGATGC 3748
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Db 4393 GCTGGATAATCTGGAGCGGGAAAGGACCACTCAGAACGCCAAGTCACCAACTGACGATGC 4452

Qy 3749 CAAGGTGATCACGGTCTCGATAAATATGGCTGAAAATGGAGAGCTGATACTGGCCAGCAA 3808
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Db 4453 CAAGGTGATCACGGTCTCGATAAATATGGCTGAAAATGGAGAGCTGATACTGGCCAGCAA 4512

Qy 3809 CCTGATGGAGAGCGAAGTGGTGCGTGTGGCCTTGACGCTAACAAAGGATCAGCCCGTCGA 3868
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Db 4513 CCTGATGGAGAGCGAAGTGGTGCGTGTGGCCTTGACGCTAACAAAGGATCAGCCCGTCGA 4572

Qy 3869 GTTGCTTCAGACGTCACTTACTAACCTGGGGATTTGCATCAAGGGCGGAAACTGTGAGCT 3928
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Db 4573 GTTGCTTCAGACGTCACTTACTAACCTGGGGATTTGCATCAAGGGCGGAAACTGTGAGCT 4632

Qy 3929 GCCCAATAAGCACTTTAGATCGATCATGCGAATGCTGCTTAACATTCTGGAGGCGGAGCA 3988
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Db 4633 GCCCAATAAGCACTTTAGATCGATCATGCGAATGCTGCTTAACATTCTGGAGGCGGAGCA 4692

Qy 3989 TACGGACGTGGTCATCGCTGGCCTGCACGTGCTCAGTAAGATTATGAGGAGCAACAAAAT 4048
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Db 4693 TACGGACGTGGTCATCGCTGGCCTGCACGTGCTCAGTAAGATTATGAGGAGCAACAAAAT 4752

Qy 4049 GCGTCACAACTGGATGCACTTTCTAGAGCTGATTTTGCTGAAGATCATCCAGTGCTATCA 4108
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Db 4753 GCGTCACAACTGGATGCACTTTCTAGAGCTGATTTTGCTGAAGATCATCCAGTGCTATCA 4812

Qy 4109 ACACAGCAAGGAGGCTTTGCGGGATATCGACTCGATGATACCAAGGATAGCACCATCCTT 4168
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Db 4813 ACACAGCAAGGAGGCTTTGCGGGATATCGACTCGATGATACCAAGGATAGCACCATCCTT 4872

Qy 4169 GCCTCTGGATCTGTCCATCAACATTGTCAATCCGGTAATTGCGACGGGTGAGTTTCCCAC 4228
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 4873 GCCTCTGGATCTGTCCATCAACATTGTCAATCCGGTAATTGCGACGGGTGAGTTTCCCAC 4932

Qy 4229 AAATTTGTGCGCCATCAAGATCCTGCTGGAAGTGACCGAACACCATGGTTCGGAGATCAC 4288
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 4933 AAATTTGTGCGCCATCAAGATCCTGCTGGAAGTGACCGAACACCATGGTTCGGAGATCAC 4992

Qy 4289 AGACGCCCACTTGGACATTGTGTTCCCCAATCTGGCGCGATCGGCGGACGACACGCAATC 4348
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Db 4993 AGACGCCCACTTGGACATTGTGTTCCCCAATCTGGCGCGATCGGCGGACGACACGCAATC 5052

Qy 4349 GATGGTTCGCAAAGCTGCGGTCTTCTGCATCGTCAAGCTGTACTTTGTTCTGGGCGAGGA 4408
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Db 5053 GATGGTTCGCAAAGCTGCGGTCTTCTGCATCGTCAAGCTGTACTTTGTTCTGGGCGAGGA 5112

Qy 4409 GAAGGTCAAGCCGAAGCTGTCAGTGCTAAATCCCAGCAAGGTTAGGCTCCTCAACGTGTA 4468
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Db 5113 GAAGGTCAAGCCGAAGCTGTCAGTGCTAAATCCCAGCAAGGTTAGGCTCCTCAACGTGTA 5172

Qy 4469 CATCGAGAAGCAGCGGAACTGCATCAGTGGGGGAGGAAGCTCTACAAAGAACTCCTCCGC 4528
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 5173 CATCGAGAAGCAGCGGAACTGCATCAGTGGGGGAGGAAGCTCTACAAAGAACTCCTCCGC 5232

Qy 4529 GGCATCGTCGTCATGATTGCGGGAGCCCTTAATAGGATTCCTGCTCGTGCCACCACAAAC 4588
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Db 5233 GGCATCGTCGTCATGATTGCGGGAGCCCTTAATAGGATTCCTGCTCGTGCCACCACAAAC 5292

Qy 4589 AAGACACAGACGCGGTTGCTTCCCTCGGCCTGAGAAGGAAGTGAGGAGCGGCGGACATTA 4648
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Db 5293 AAGACACAGACGCGGTTGCTTCCCTCGGCCTGAGAAGGAAGTGAGGAGCGGCGGACATTA 5352

Qy 4649 AATAATATATTATTACATTAACTAATTATTTATAACTAATTATTACCGATCATCCGTTAC 4708
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Db 5353 AATAATATATTATTACATTAACTAATTATTTATAACTAATTATTACCGATCATCCGTTAC 5412

Qy 4709 TTGTGTAACTGCTCGATGCATATATTCAGCAGATGCAAATGCGGCCCGAAAGAAAGTCAA 4768
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Db 5413 TTGTGTAACTGCTCGATGCATATATTCAGCAGATGCAAATGCGGCCCGAAAGAAAGTCAA 5472

Qy 4769 GGGCCATCGCCCATCTAATGTGAGCAGAAAAACTATTTATACATAAACGGGAACTAAAGC 4828
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Db 5473 GGGCCATCGCCCATCTAATGTGAGCAGAAAAACTATTTATACATAAACGGGAACTAAAGC 5532

Qy 4829 GAGTAAATCCGCAAAGTGTACTAAAATTGTAGCCAACTCCGCAATCCTCACTTCTCACAT 4888
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 5533 GAGTAAATCCGCAAAGTGTACTAAAATTGTAGCCAACTCCGCAATCCTCACTTCTCACAT 5592

Qy 4889 CAGTTGTACGTCTTTTTACCAGCTCCTAACTATTAACGCTGATTCTGTTTAATTTGTAAG 4948
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 5593 CAGTTGTACGTCTTTTTACCAGCTCCTAACTATTAACGCTGATTCTGTTTAATTTGTAAG 5652
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Qy 4949 CCTATATACCGCTCTTTATGGAAACTCAGACGTGTGCTTTTCTACCTTTGTTTCAGGCGA 5008
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Db 5653 CCTATATACCGCTCTTTATGGAAACTCAGACGTGTGCTTTTCTACCTTTGTTTCAGGCGA 5712

Qy 5009 CTTTGTATCCTTATTTCGTTTCCGCTCAACTAAATTCTAATTACTATTATTAATACGATT 5068
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Db 5713 CTTTGTATCCTTATTTCGTTTCCGCTCAACTAAATTCTAATTACTATTATTAATACGATT 5772

Qy 5069 CTGCTCTTACAACTGAACTATTTTTGTAATTAATTTAAATACACAAGCCCACACAAAGGA 5128
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Db 5773 CTGCTCTTACAACTGAACTATTTTTGTAATTAATTTAAATACACAAGCCCACACAAAGGA 5832

Qy 5129 TTAAAATCAATAAAAAA 5145
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Db 5833 TTAAAATCAATAAAAAA 5849
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Claims 3-4, 7-8 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Homburger et al. (US 6,703,491, 1999).

Homburger et al. teach an isolated polynucleotide that is 98.7% identical from nucleotides 2639 to 3408 of the instantly claimed polynucleotide of SEQ ID NO: 1 (see attached sequence comparison). Moreover, the patent teaches DNA probes derived from genomic DNA or cDNAs of the genes which can be used to detect transposition events that rearrange the genomic DNA of the genes (column 37, line 65 to column 38, line1). The patent further teaches vectors expression vectors and host cells comprising the nucleic acids (abstract, column 24, line 57+ and column 26, line 60+). Thus, while Homburger et al. does not explicitly teach that the nucleotide sequence is cabable of hybridizing to the nucleotide set forth in SEQ ID NO: 1, the claimed limitation does not appear to result in a manipulative difference because the specification teaches (page 15, lines 13-20) that polynucleotides of the invention capable of selectively hybridizing to the nucleotide sequences represented herein, or to their complement, will be generally at least 70%, preferably at least 80% or 90% and more preferably at least 95% or 98% homologous to the corresponding nucleotide sequences presented herein over a region of at least 20, preferably at least 25 or 30, for instance at least 40, 60 or 100 or more contiguous nucleotides. As such, Homburger et al.'s nucleotide which is 98.7% identical over at least 100 contiguous nucleotides meets the limitation. Furthermore, while Homburger et al.'s do not explicitly recite that the polynucleotide can be used in therapy, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition

is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Claim 1-2 is rejected under 35 U.S.C. 102(b) as being anticipated by NCBI database for single nucleotide polymorphism (National Center for Biotechnology Information, National Library of Medicine, NIH (Bethesda, MD, USA), IDS) having the accession # AB014522 submitted on 2/06/1999.

The NCBI database provides a polynucleotides which encodes a polypeptide that has 18.1% identity and 30.1% local similarity from amino acids 236 to 1492 of orbit, i.e., the amino acid sequence of SEQ ID NO: 2. Specifically, the NCBI database teaches that the polynucleotide is isolated from the human brain. Thus, while the NCBI database does not explicitly teach that the polynucleotide molecule encodes an orbit homolog such as human orbit, the claimed limitation does not appear to result in a manipulative difference because the specification teaches that homologous sequences are taken to include an amino acid sequence that is at least 15, 20, 25, 30, 40, 50, 60, 70, 80 or 90% identical, preferably 95 or 98% identical at the amino acid level over at least 50 or 100, preferably 200, 300, 400 or 500 amino acids with SEQ ID NO: 2 (page 7, lines 22-25). As such, the NCBI database's polynucleotide which encodes a polypeptide 30.1% similar to over at least 500 amino acids of SEQ ID NO: 2 meets the limitation of an orbit homologue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-8 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over NCBI database for single nucleotide polymorphism (National Center for Biotechnology Information, National Library of Medicine, NIH (Bethesda, MD, USA), IDS) having the accession # AB014522

submitted on 2/06/1999 in further view of Alberts *et al.* (Molecular Biology of the Cell, 3rd edition, 1994, pages 320-321).

The NCBI database provides, as applied to claims 1-2 above, a polynucleotides which encodes a human homologue of orbit, wherein the polypeptide has 18.1% total identity and 30.1% local similarity from amino acids 236 to 1492 of orbit, i.e., the amino acid sequence of SEQ ID NO: 2.

The NCBI database does not explicitly teach a vector or expression vector comprising said polynucleotide. Moreover, the NCBI database does not explicitly teach a host cell which comprises an expression vector.

Alberts et al. teach that rare cellular protein can be made in large amounts using expression vectors (page 320, Heading). Specifically, the reference teaches that while first synthesizing a large amount of mRNA that encodes a protein and translating it in a cell free system is occasionally used, a more efficient way to produce both mRNA and the protein is in a living cell, wherein a vector is designed to produce a large amount of mRNA that will be efficiently translated into protein in the transfected bacterial, yeast, insect or mammalian cell (page 320, last paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a vector/expression vector comprising the polynucleotide in a host cell as taught by the NCBI database in view of Alberts et al. teachings that expression vectors are an efficient way of producing large amounts of protein. One would have been motivated to do so because Alberts et al. teaches that until recently, the only proteins in a cell that could be studied easily were relatively abundant ones (page 320, 3rd full paragraph). Thus, one of ordinary skill in the art would have a reasonable expectation that by using a vector/expression vector comprising the polynucleotide in a host cell as taught by the NCBI database, one would achieve a an efficient way to synthesize large amounts of the protein for structure and function determinations.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF
5/4/2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER